Notice of Allowability	Application N .	Applicant(s)	
	09/680,738	EDWARDS ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed August 25, 2003*.
2. ☒ The allowed claim(s) is/are *22-25*.
3. ☒ The drawings filed on *09 June 2002* are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.
5. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
   (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

8. ☐ CORRECTED DRAWINGS must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No. ____.
   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
   (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachm nt(s)

1☐ Notice of References Cited (PTO-892)
2☐ Notice of Informal Patent Application (PTO-152)
3☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
4☒ Interview Summary (PTO-413), Paper No. *1103* .
5☐ Information Disclosure Statements (PTO-1449), Paper No. ____.
6☒ Examiner's Amendment/Comment
7☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
8☐ Examiner's Statement of Reasons for Allowance
9☐ Other .

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mar on November 4, 2003.

Please note that reference US 5,925,523 has been crossed through on the form PTO-892 mailed August 1, 2001. This is because the reference is a duplication of a reference cited on a form PTO-1449, and has already been considered on the record.

The application has been amended as follows:

In the claims:

Please cancel claims 1, 10, 11 and 17. Please add the following claims.

22. A method for detecting an interaction between a first test protein and a second test protein at variable sensitivities via a detectable reporter gene, the method comprising:

providing a host cell wherein the host cell comprises a detectable reporter gene capable of expressing a detectable reporter gene product;

providing to the host cell a first hybrid protein comprising a polypeptide region capable of binding DNA and a bait polypeptide derived from the first test protein and a second hybrid

protein comprising a polypeptide region capable of transcriptional activation and a prey polypeptide derived from the second test protein, wherein the host cell is additionally provided with the capacity to regulate the absolute or relative amounts of the first and second hybrid proteins;

regulating the amounts of the first and second hybrid proteins in a continuously adjustable manner so the detectable reporter gene is activated; and

determining the extent to which the detectable reporter gene has been activated whereby an interaction between the first test protein and the second test protein is detected,

wherein the first or second hybrid protein is provided by introducing into the host cell a first or second chimeric gene capable of being expressed in the host cell,

wherein the first chimeric gene comprises a first exogenously activatable promoter, a sequence coding for a DNA binding region or polypeptide, and a sequence coding for the bait polypeptide,

wherein the first exogenously activatable promoter is activated by a first exogenous activator, and

wherein the first exogenous activator includes a natural or synthetic metabolically active or inactive steroid, steroid analog or steroid mimic.

23. A method for detecting an interaction between a first test protein and a second test protein at variable sensitivities via a detectable reporter gene, the method comprising:

providing a host cell wherein the host cell comprises a detectable reporter gene capable of expressing a detectable reporter gene product;

providing to the host cell a first hybrid protein comprising a polypeptide region capable of binding DNA and a bait polypeptide derived from the first test protein and a second hybrid protein comprising a polypeptide region capable of transcriptional activation and a prey polypeptide derived from the second test protein, wherein the host cell is additionally provided with the capacity to regulate the absolute or relative amounts of the first and second hybrid proteins;

regulating the amounts of the first and second hybrid proteins in a continuously adjustable manner so the detectable reporter gene is activated; and

determining the extent to which the detectable reporter gene has been activated whereby an interaction between the first test protein and the second test protein is detected,

wherein the first or second hybrid protein is provided by introducing into the host cell a first or second chimeric gene capable of being expressed in the host cell,

wherein the second chimeric gene comprises a second exogenously activatable promoter, a sequence coding for a transcriptional activation domain or polypeptide, and a sequence coding for the prey polypeptide,

wherein the second exogenously activatable promoter is activated by a second exogenous activator, and

wherein the second exogenous activator includes a natural or synthetic metabolically active or inactive steroid, steroid analog or steroid mimic.

24. The method of one of Claims 22 or 23 wherein at least one of the first or second exogenous activators is chosen from the group consisting of cortisol, hydrocortisone, estrogen, estradiol,

estrone, progesterone, androgen, ecdysone, retinoid, steroids which bind to orphan receptors, mineralocorticoid and mineralocorticoid analogues, and combinations thereof.

25. A method for detecting an interaction between a first test protein and a second test protein at variable sensitivities via a detectable reporter gene, the method comprising:

providing a host cell wherein the host cell comprises a detectable reporter gene capable of expressing a detectable reporter gene product;

providing to the host cell a first hybrid protein comprising a polypeptide region capable of binding DNA and a bait polypeptide derived from the first test protein and a second hybrid protein comprising a polypeptide region capable of transcriptional activation and a prey polypeptide derived from the second test protein, wherein the host cell is additionally provided with the capacity to regulate the absolute or relative amounts of the first and second hybrid proteins;

regulating the amounts of the first and second hybrid proteins in a continuously adjustable manner so the detectable reporter gene is activated; and

determining the extent to which the detectable reporter gene has been activated whereby an interaction between the first test protein and the second test protein is detected,

wherein the host cell is from Saccharomyces cerevisiae strain comprising three integrated promoters for the detection of two-hybrid interactions, the first integrated reporter being a construct yielding a quantifiable product, the second and third integrated reporters being constructs yielding proteins sufficient to rescue nutrient auxotrophies,

wherein the first hybrid protein is provided by

introducing into the host cell a plasmid containing an ampicillin or kanamycin resistance gene, a colE1 origin of replication and a DNA sequence encoding a first hybrid protein comprising a bait polypeptide and a Gal4p DNA binding domain, the expression of which is controlled by an integrated estrogen-inducible promoter; and

inducing expression of the first hybrid protein by incubating the host cell with an exogenous activator capable of activating the promoter, and

wherein the second hybrid protein is provided by

introducing into the host cell a plasmid containing an ampicillin or kanamycin resistance gene, a colE1 origin of replication and a DNA sequence encoding a second hybrid protein comprising a prey polypeptide derived from a library and the carboxy-terminal end of the Gal4p transcriptional activation domain, the expression of which is controlled by a rat glucocorticoid-inducible promoter; and

inducing expression of the second hybrid protein by incubating the host cell with an exogenous activator capable of activating the promoter.

Note: Claims 1, 10, 11 and 17 were cancelled for purposes of entering the Examiner's amendment. The Examiner's Amendment was necessary because the previous amendment to the claims was technically Non-Responsive. For the sole purpose of furthering prosecution, the amendment was entered in order to avoid sending a Notice of Non-Responsiveness; the claim language is identical with the exception of a correction in the spelling of "steroid" as indicated in claim 10.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
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JAMES KETTER
PRIMARY EXAMINER